

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (Currently Amended). A method for treating conditions wherein TNF, either endogenously formed or exogenously administered, is to be eliminated from the body or its effect in the body is to be antagonized, comprising administering to a patient in need of such treatment an effective amount of a pharmaceutically acceptable composition, the active ingredient of which is a protein,~~which had previously been substantially purified,~~ capable of interacting with TNF so as to inhibit the binding of TNF to cells and to inhibit the cytotoxic effect of TNF, said protein comprising the following amino acid sequence:

Asp-Ser-Val-Cys-Pro-Gln-Gly-Lys-Tyr-Ile-His-Pro-Gln-X-Asn-Ser
(SEQ ID NO:1)

wherein X is an unidentified amino acid residue.

2 (Currently Amended). A method for reducing the cytotoxic activity of TNF, comprising bringing into contact with TNF a pharmaceutically acceptable composition, the active ingredient of which is a protein,~~which had previously been substantially purified,~~ capable of interacting with TNF so as to inhibit the binding of TNF to cells and to inhibit the

cytotoxic effect of TNF, said protein comprising the following amino acid sequence:

Asp-Ser-Val-Cys-Pro-Gln-Gly-Lys-Tyr-Ile-His-Pro-Gln-X-Asn-Ser
(SEQ ID NO:1)

wherein X is an unidentified amino acid residue.

3 (Currently Amended). A method for treating conditions wherein TNF, either endogenously formed or exogenously administered, is to be eliminated from the body or its effect in the body antagonized, comprising administering to a patient in need of such treatment an effective amount of a pharmaceutically acceptable composition, the active ingredient of which is a protein, ~~which had previously been substantially purified,~~ or a fragment thereof capable of inhibiting the binding of TNF to cells and of inhibiting the cytotoxic effect of TNF, wherein said protein is obtainable from human urine and has the following features:

(a) it is a protein that does not have proteolytic activity, capable of interacting with TNF so as to inhibit the binding of TNF to cell surface receptors and to inhibit the cytotoxic effect of TNF;

(b) the major peak of TNF inhibiting activity elutes slightly before the majority of the protein and shows an apparent molecular weight of about 40-80 kDa when measured as

a crude urine concentrate chromatographed on an Ultrogel AcA 44 filtration column; and

(c) the isoelectric point of the active protein is between pH 6 and 8, when measured as a crude urine concentrate analyzed by electro-focusing.

4 (Currently Amended). A method for treating conditions wherein TNF, either endogenously formed or exogenously administered, is to be eliminated from the body or its effect in the body antagonized, comprising administering to a patient in need of such treatment an effective amount of a pharmaceutically acceptable composition, the active ingredient of which is a molecule ~~which had previously been substantially purified,~~ capable of inhibiting the binding of TNF to cells and of inhibiting the cytotoxic effect of TNF, wherein said molecule comprises a polypeptide having the sequence of a protein obtainable from human urine and having the following features:

(a) it is a protein that does not have proteolytic activity, capable of interacting with TNF so as to inhibit the binding of TNF to cell surface receptors and to inhibit the cytotoxic effect of TNF;

(b) the major peak of TNF inhibiting activity elutes slightly before the majority of the protein and shows an apparent molecular weight of about 40-80 kDa when measured as

a crude urine concentrate chromatographed on an Ultrogel AcA 44 filtration column; and

(c) the isoelectric point of the active protein is between pH 6 and 8, when measured as a crude urine concentrate analyzed by electro-focusing,

or a salt, functional derivative or active fragment of said polypeptide, which salt, functional derivative or active fragment is capable of inhibiting the binding of TNF to cells and of inhibiting the cytotoxic effect of TNF.

5 (Cancelled).

6 (Currently Amended). A method for treating conditions wherein TNF, either endogenously formed or exogenously administered, is to be eliminated from the body or its effect in the body antagonized, comprising administering to a patient in need of such treatment an effective amount of a pharmaceutically acceptable composition, the active ingredient of which is a polypeptide, ~~which had previously been substantially purified,~~ capable of interacting with TNF so as to inhibit the binding of TNF to its receptors and to inhibit the cytotoxic effect of TNF, said polypeptide comprising the amino acid sequence Asp-Ser-Val-Cys-Pro-Gln-Gly-Lys-Tyr-Ile-His-Pro-Gln-X-Asn-Ser, where X is an unidentified amino acid residue, functional derivatives or

active fractions thereof, said active fraction being a fragment of the polypeptide chain of the isolated polypeptide alone or together with associated molecules or residues linked thereto and having the ability to inhibit the binding of TNF to its receptors and to inhibit the cytotoxic effect of TNF.

7 (Currently Amended). A method for reducing the cytotoxic activity of TNF, comprising bringing into contact with TNF a pharmaceutically acceptable composition, the active ingredient of which is a protein, which had previously been substantially purified, or a fragment thereof capable of inhibiting the binding of TNF to cells and of inhibiting the cytotoxic effect of TNF, wherein said protein is obtainable from human urine and has the following features:

(a) it is a protein that does not have proteolytic activity, capable of interacting with TNF so as to inhibit the binding of TNF to cell surface receptors and to inhibit the cytotoxic effect of TNF;

(b) the major peak of TNF inhibiting activity elutes slightly before the majority of the protein and shows an apparent molecular weight of about 40-80 kDa when measured as a crude urine concentrate chromatographed on an Ultrogel AcA 44 filtration column; and

(c) the isoelectric point of the active protein is between pH 6 and 8, when measured as a crude urine concentrate analyzed by electro-focusing.

8 (Currently Amended). A method for reducing the cytotoxic activity of TNF, comprising bringing into contact with TNF a pharmaceutically acceptable composition, the active ingredient of which is a molecule, which had previously been substantially purified, capable of inhibiting the binding of TNF to cells and of inhibiting the cytotoxic effect of TNF, wherein said molecule comprises a polypeptide having the sequence of a protein obtainable from human urine and having the following features:

(a) it is a protein that does not have proteolytic activity, capable of interacting with TNF so as to inhibit the binding of TNF to cell surface receptors and to inhibit the cytotoxic effect of TNF;

(b) the major peak of TNF inhibiting activity elutes slightly before the majority of the protein and shows an apparent molecular weight of about 40-80 kDa when measured as a crude urine concentrate chromatographed on an Ultrogel AcA 44 filtration column; and

(c) the isoelectric point of the active protein is between pH 6 and 8, when measured as a crude urine concentrate analyzed by electro-focusing,

or a salt, functional derivative or active fragment of said polypeptide, which salt, functional derivative or active fragment is capable of inhibiting the binding of TNF to cells and of inhibiting the cytotoxic effect of TNF.

9 (Cancelled).

10 (Currently Amended). A method for reducing the cytotoxic activity of TNF, comprising bringing into contact with TNF a pharmaceutically acceptable composition, the active ingredient of which is a polypeptide, which had previously been substantially purified, capable of interacting with TNF so as to inhibit the binding of TNF to its receptors and to inhibit the cytotoxic effect of TNF, said polypeptide comprising the amino acid sequence Asp-Ser-Val-Cys-Pro-Gln-Gly-Lys-Tyr-Ile-His-Pro-Gln-X-Asn-Ser, where X is an unidentified amino acid residue, functional derivatives or active fractions thereof, said active fraction being a fragment of the polypeptide chain of the isolated polypeptide alone or together with associated molecules or residues linked thereto and having the ability to inhibit the binding of TNF to its receptors and to inhibit the cytotoxic effect of TNF.